

U.S. Serial No. 10/759,519

Amendment responsive to 4/12/2006 Office Action

Amendment dated October 12, 2006

RECEIVED
CENTRAL FAX CENTER

OCT 12 2006

Amendments to the specification:

Please amend paragraph [021] as follows:

[021] In one embodiment, the invention provides a method of determining a haplotype in a sample obtained from an organism and comparing it to known haplotypes to diagnose a disease or disease susceptibility of an organism comprising the steps of identifying at least two polymorphic markers within a genomic region; isolating a nucleic acid sample from the subject organism and preferably purifying the isolated nucleic acid; diluting the nucleic acid sample into substantially single molecule dilution; amplifying the diluted nucleic acid sample with at least two primer pairs each capable of amplifying a different region flanking each of the polymorphic sites in a multiplex PCR reaction; genotyping the polymorphic sites from the amplified sample; producing at least three additional genotype replicas from the nucleic acid sample of the subject organism as described above to allow statistically accurate determination of the haplotype in the subject organism sample. In a preferred method the genotyping is performed using primer extension, terminator nucleotides and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry MALDI-TOF MS analysis. The haplotype is thereafter compared to an existing haplotype collection such as a haplotype database comprising disease- or disease susceptibility-associated haplotypes, or haplotypes associated with treatment responsiveness or unresponsiveness of the specific polymorphic markers. An non-limiting example of an existing haplotype database is a Y-STR Haplotype Reference Database which can be found at http://ystr.charite.de/index_gr.html.

Please amend paragraph [051] as follows:

[051] Polymorphic Markers and Oligonucleotides. The number of polymorphic nucleic acid useful according to the present invention is ever increasing. Currently, such markers are readily available from a variety of publicly accessible databases and new ones are constantly being added to the pool of available markers. Markers including restriction length polymorphisms, short tandem repeats such as di-, tri-, and tetra-nucleotide repeats as well as methylation status can be used as polymorphic markers according to the present invention. Such markers are well known to one skilled in the art and can be found in various publications and databases including, for example, ATCC short tandem repeat (STR) database at <http://www.atcc.org/Cultures/str.cfm>.

U.S. Serial No. 10/759,519
Amendment responsive to 4/12/2006 Office Action
Amendment dated October 12, 2006

Please amend paragraph [052] as follows:

[052] Particularly useful markers according to the present invention are single nucleotide polymorphisms (SNPs). Examples of useful SNP databases include, but are not limited to Human SNP Database at Whitehead Institute, MIT <http://www.genome.wi.mit.edu/snp/human>, NCBI dbSNP Home Page at NIH databases <http://www.ncbi.nlm.nih.gov/SNP>, Lifesciences/Perkin Elmer SNP database <http://lifesciences.perkinelmer.com/SNPDatabase/welcome.asp>, Celera Human SNP database at <http://www.celera.com/genomics/academic/home.cfm?ppage=eds&epage=snp>, and the SNP Database of the Genome Analysis Group (GAN) at <http://www.gan.iarc.fr/SNPdatabase.html>.